STATUS OF CLAIMS

1-13 (canceled)

14. (previously amended) A method for validating the effect of a candidate gene that is expressed in a mammalian neural cell of interest, said method comprising:

(a) producing a candidate dsRNA which comprises at least 100 nucleotides of said candidate gene;

(b) introducing said candidate dsRNA into a reference mammalian neural cell; and

(c) validating the effect of said candidate gene by detecting an alteration in a cellular activity or a cellular state in said reference mammalian neural cell, wherein said alteration is the result of specific attenuation of mRNA corresponding to said candidate in said reference mammalian neural cell, indicating that said candidate gene plays a functional role in mammalian neural cells.

15. (previously amended) The method of claim 14, wherein said step of producing the candidate dsRNA comprises:

producing a cDNA corresponding to said candidate gene from an mRNA of said mammalian neural cell of interest; and producing the candidate dsRNA from said cDNA.

16. (canceled)

17. (previously amended) The method according to Claim 15, further comprising:

producing a plurality of candidate cDNAs from said mammalian neural cell of interest;

producing a plurality of candidate dsRNA which comprise at least 100 nucleotides of said candidate cDNAs;

introducing each of the candidate dsRNA into a plurality of separate reference mammalian neural cells having a gene expression similar to said mammalian neural cell of interest;

and validating the effect of said candidate genes by testing for alterations in a cellular activity or a cellular state in said reference mammalian neural cell that result of attenuation of mRNA corresponding to said candidate in said reference mammalian neural cell, wherein detection of said alterations is indicative that said candidate gene plays a functional role in said mammalian neural cells of interest.

18. (canceled)

19. (previously amended) The method of claim 17, wherein said step of producing a plurality of candidate cDNAs comprises:

producing double-stranded cDNA from mRNA by reverse transcription;

producing cDNAs of a similar length by digesting said cDNA with a restriction enzyme; and

producing a plasmid or PCR fragment from said cDNA after said digesting step.

20. (previously amended) The method of claim 19, wherein the candidate dsRNA is produced by transcribing said plasmid cDNA or PCR fragment.

21. (canceled)

22. (original) The method of claim 19, wherein the restriction enzyme is selected from the group consisting of Dpn1 and Rsa1.

23. (previously amended) The method of claim 17, wherein said step of producing the plurality of candidate dsRNAs comprises: selecting a candidate cDNA that is expressed at a detectably different level with respect to said reference mammalian neural cell and said mammalian neural cell of interest, and said reference mammalian neural cell and said mammalian neural cell of interest differ with respect to a cellular characteristic that is detectable by said step of testing for alterations in a cellular activity or a cellular state.

24. (previously amended) The method of claim 23, wherein the candidate cDNA is selected from a normalized library prepared from said reference mammalian neural cells or said mammalian neural cell of interest and is present in low abundance in the normalized library.

25. (previously amended) The method of claim 23, wherein the candidate cDNA is a differentially expressed cDNA selected from a subtracted library that is enriched for cDNAs that are differentially expressed with respect to said reference mammalian neural cells or said mammalian neural cell of interest.

26. (canceled)

27. (previously amended) The method of claim 23, wherein said step of selecting the candidate cDNA comprises:

preparing a tester-normalized cDNA library from test cells; a driver-normalized cDNA library from control cells; a tester-subtracted cDNA library which is enriched in one or more genes that are up-regulated with respect to the test cell and the control cell, and a driver-subtracted cDNA library which is enriched in one or more genes that are down-regulated with respect to the test cell and the control cell; and

selecting a cDNA from the normalized libraries by contacting cDNAs from the tester-normalized cDNA library with labeled probes derived from mRNA from test cells and contacting cDNAs from the driver-normalized cDNA library with labeled probes derived from mRNA from control cells under conditions whereby probes specifically hybridize with complementary cDNAs to form a first set of hybridization complexes; and detecting at least one hybridization complex from the first set of hybridization complexes to identify a cDNA that is present in low abundance.

28. (canceled)

29. (previously amended) The method of claim 23, wherein said step of selecting the candidate cDNA comprises:

preparing a tester-normalized cDNA library from test cells; a driver-normalized cDNA library from control cells; a tester-subtracted cDNA library which is enriched in one or more genes that are up-regulated with respect to the test cell and the control cell, and a driver-subtracted cDNA library which is enriched in one or more genes that are down-regulated with respect to the test cell and the control cell; and

selecting a cDNA from the subtracted libraries by contacting cDNAs from the tester-subtracted cDNA library and contacting cDNAs from the driver-subtracted cDNA library with a population of labeled probes under conditions whereby probes from the population of probes specifically hybridize with complementary cDNAs to form a second set of hybridization complexes, and wherein the population of labeled probes is derived from mRNA from test cells and control cells; and detecting at least one hybridization complex from the second set of hybridization complexes to identify a cDNA that is differentially expressed above a threshold level with respect to the subtracted libraries.

30. (previously amended) The method of claim 23, wherein the cellular characteristic is cell health, the test cell is a diseased neural cell and the control cell is a healthy neural cell, and the candidate gene is suspected of correlation with a disease.

31. (original) The method of claim 30, wherein the test cell is obtained from a mammal that has had a stroke or is at risk for stroke.

32-33. (canceled)

34. (previously amended) The method of claim 23, wherein the cellular characteristic is cellular differentiation and the candidate gene is suspected of correlation with control of cellular differentiation.

35. (previously amended) The method of claim 23, wherein the candidate gene is endogenous to said mammalian neural reference cell.

36. (previously amended) The method of claim 23, wherein the candidate gene is an extrachromosomal gene in said mammalian neural reference cell.

37-42 (canceled)

43. (previously amended) The method of claim 30, wherein said mammalian neural reference cell is a neuroblastoma cell.

44. (canceled)

45. (previously amended) The method of claim 44, wherein said mammalian neural reference cell has increased sensitivity to N-methyl-D-aspartate, β-amyloid, peroxide, oxygen-glucose deprivation, or combinations thereof, relative to a normal mammalian neural cell.

46. (previously amended) The method of claim 45, wherein the detecting step comprises detecting a decrease in cellular sensitivity to N-methyl-D-aspartate, β-amyloid, peroxide, oxygen-glucose deprivation, or combinations thereof, relative to a normal mammalian neural cell.

47. (original) The method of claim 17, wherein the detecting step comprises detecting modulation of ligand binding to a protein.

48-50 (canceled)

51. (previously amended) The method of claim 14, wherein the determining step comprises determining whether the protein encoded by the candidate gene binds to another protein to form a coimmunoprecipitating complex.

52. (previously added) The method of claim 14, wherein the candidate dsRNA is at least 500 nucleotides in length.

53. (previously added) The method of claim 14, wherein the candidate dsRNA is between 500 and 1100 nucleotides in length.

54. (previously added) The method of claim 14, wherein said mammalian neural cell of interest is a glial cell.

55. (previously added) The method of claim 14, wherein said reference mammalian neural cell is a glial cell.